## REMARKS

As a preliminary matter, please note and make the necessary changes to reflect that the docket number for this application has changed from 441842000401 to 49123.000025.UTL1.

In the Office Action dated May 28, 2003, the Patent Office indicated that claims 30-33, and 37-40 are directed to allowable subject matter.

Claims 1-35 were originally filed in the instant application. Claims 37-40 were added by a preliminary amendment dated March 17, 2003. Claims 1-26 and 36 are drawn to a non-elected invention and have been withdrawn by the Patent Office. In this response, claims 1-26 and 36 have been canceled. Claims 27-35 and 37-40 are therefore pending. In this response, paragraph 0056 of the specification has been replaced to correct the spelling of the word "ferrocytocheome" to read "ferrocytochrome". No new matter has been added by the addition of the new claims, full support being found throughout the originally filed specification, claims, and drawings.

***Rejections under 35 U.S.C. §112, Second Paragraph***

Claims 27-35 and 37-40 stand rejected under 35 U.S.C. §112, second paragraph.

Claim 27

The Office Action alleges that claim 27 is indefinite because "It is unclear if fructosamine oxidase is used to measure the product formation or if the reaction be measured is catalyzed by fructosamine oxidase." (Emphasis added). Applicant traverses this rejection.

This rejection is deficient under the law. The Patent Office has not provided any rationale to support its position that claim 27 on its face would be understood by one of skill in the art to have a meaning in accordance with the above hypothetical first interpretation. To start, the grammar of claim 27 is inconsistent with the above first interpretation. Claim 27 places the verb "measuring" directly before the phrase "conversion of a substrate to a product". The

grammar and organization of claim 27 makes clear that what is measured is "the conversion of a substrate to a product". Applicant respectfully submits that the Examiner's suggestion of inserting the word "catalysed" after "product", which in itself evidences that the Examiner correctly understands claim 27 as currently drafted, merely reflects the Examiner's personal preference but is not needed or required.

It is well settled that determining whether a claim is indefinite requires an analysis of "whether one skilled in the art would understand the bounds of the claim when read in light of the specification. . . If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, [section] 112 demands no more." *Miles Lab., Inc. v. Shandon Inc.*, 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993), *cert. denied*, 114 S. Ct. 943 (1994); see also *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). Further, the Manual of Patenting Examining Procedure (MPEP) provides the following guidance: "The examiner's focus during examination of claims for compliance with the requirement for definiteness. . . is whether the claim meets the threshold requirement for clarity and precision, not whether more suitable language or modes of expression are available." M.P.E.P. § 2173.02 (8th ed. 2001)(emphasis added).

The Patent and Trademark Office has also erred in failing to consider how one of skill in the art would interpret claim 27 in light of the specification. Applicant is unable to find any description or embodiment in the specification of the instant application that supports the interpretation hypothesized by the Patent Office that "fructosamine oxidase is used to measure the product formation." Instead, the teachings of the instant specification clearly go against this hypothetical interpretation. See for example, paragraph 0051 of the instant application published

as 2002/0034775 stating: "Fructosamine oxidase catalyses the degradation of fructosamine(s) with concurrent reduction of molecular oxygen yielding a superoxide reaction product (FIG. 1)" (emphasis added), and paragraph 0056 which states: "Fructosamine oxidase activity may be measured using the redox-active color reagent, ferricytochrome C, which is readily reduced by superoxide to form ferrocytocheome c with a characteristic increase in absorbance at 550 nM." To summarize, in light of the instant specification one of skill in the art would not misconstrue the plain language of claim 27 to consider the scope of the claim indefinite for the reasons suggested by the Patent Office. The Patent and Trademark Office has failed to meet the legal burden required to establish a *prima facie* case of indefiniteness under 35 U.S.C. §112, second paragraph. Accordingly, Applicant respectfully request that the rejection of claim 27 under 35 U.S.C. §112, second paragraph be reconsidered and withdrawn.

Claims 28-29

The Patent Office alleges that it is unclear what applicant means by "superoxide reaction product" or "oxygen free radical reaction product" in claims 28 and 29.

The Examiner is reminded that a claim is not required to provide a written description of the invention in order to be considered definite under Section 112, second paragraph. Rather, the specification is required to describe the invention so that "persons of ordinary skill in the art will recognize from the disclosure that applicants invented processes including those limitations." *In re Wertheim*, 541 F.2d 257, 191 USPQ 90, 96 (C.C.P.A. 1976) (citing *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284 (C.C.P.A. 1973)). Likewise, a claim is not required to enable one of ordinary skill in the art to make and use the invention to be considered definite under Section 112, second paragraph. Rather, the specification is required to "describe the invention ... in such detail as to enable a person skilled in the most relevant art to make and use it." *In re*

*Naquin*, 398 F.2d 863, 158 USPQ 317, 319 (C.C.P.A. 1968) (citing *International Standard Elec. Corp. v. Ooms*, 157 F.2d 73, 70 USPQ 32 (D.C. Cir. 1946)); see also *Miles Lab., Inc. v. Shandon Inc.*, 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993), *cert. denied*, 114 S. Ct. 943 (1994).

A description of "superoxide reaction product" and "oxygen free radical reaction product" is present in the instant specification. For example, in Figure 1 and in paragraph 0051 of US2002/0034775 stating "Fructosamine oxidase catalyses the degradation of fructosamine(s) with concurrent reduction of molecular oxygen yielding a superoxide reaction product (FIG. 1). Superoxide is unstable in aqueous solution with spontaneous dismutation to hydrogen peroxide and oxygen." (Emphasis added). Figure 1 diagrams the substrates and end products of the reaction, including the conversion of $O_2$ to $O_2^{(-)}$.

In light of the clear teachings of the instant specification and analysis and law referenced hereinabove, Applicant traverses this rejection and respectfully requests that this rejection be reconsidered and withdrawn.

Claim 30

The Office Action states "Claim 30, where is the mechanism disabled? Presumably in the sample taken for the determination of fructosamine oxidase activity". The Examiner's attention is drawn to paragraph 0054 of the specification which clearly and plainly teaches inhibition of SOD activity in a plasma sample. Claim 30 is definite in light of the instant specification. Accordingly, with reference to the legal authority and analysis referenced herein above, Applicant traverses this rejection and respectfully requests that this rejection be reconsidered and withdrawn.

Claims 31 and 32

For the sole purpose of expediting prosecution and with no prejudice or admission that this rejection was proper, claims 31 and 32 have been reworded as suggested by the Examiner to read: to "the substrate" instead of "suitable fructosamine substrate". This is clearly not a narrowing amendment because claim limitations have been removed. As such, this revision cannot be construed to narrow the appropriate scope of claim 31 or 32 under the principles of claim interpretation or the doctrine of equivalents.

The Patent Office also alleges that claim 31 has no antecedent basis for "the exposure". The phrase "the exposure" is an inherent property of the method for which explicit antecedent support is not necessary. See M.P.E.P. 2173.05(e) citing *Ex parte Porter*, 25 USPQ2d 1144, 1145 (Bd. Pat. App. & Inter. 1992). The Patent Office has not suggested alternative claim language to correct the alleged antecedent basis problem (see M.P.E.P. 2173.05(e) indicating such a suggestion is appropriate). Nonetheless, for the sole purpose of expediting prosecution and with no prejudice or admission that this rejection was proper, Applicant has removed the word "the" before "exposure". Again, this is not a narrowing amendment because removing the word "the" does not narrow the scope of claim 31. Accordingly, this revision cannot be construed to narrow the appropriate scope of claim 31 under the principles of claim interpretation or the doctrine of equivalents.

Applicant respectfully request that the rejections of claims 31 and 32 under 35 U.S.C. §112, second paragraph be withdrawn.

***Rejections under 35 U.S.C. §102(b)***

Claims 27-29, 34, and 35 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Hourichi et al. The Office Action states:

> "Hourichi et al. disclose a method for assaying fructosyl-amino acid oxidase (E.C. 1.5.3) comprising: adding fructosyl-glycine to the oxidase in a buffer ... and measuring glycine and glycosone and hydrogen peroxide, the products of the reaction..." (emphasis added).

Applicant traverses the rejections under 35 U.S.C. §102(b) over Hourichi et al. because the enzyme taught in Hourichi et al is a different enzyme than the novel fructosamine oxidase of the instant invention (claim 27).

To begin, the names of the two enzymes are different. The Patent Office acknowledges that Hourichi et al. is directed to a fructosyl-amino acid oxidase. On page 108 of Hourichi et al., the authors comment that their enzyme's "systematic name should be fructosyl-a-L-amino acid: oxygen oxidoreductase (defructosylating)." The underlined portion of the name of the enzyme taught in Hourichi et al. (fructosyl-amino acid oxidase) highlights a primary distinction in the nomenclature. The "amine" embedded within the claimed fructosamine oxidase is clearly not the same as the "amino acid" embedded within the name of the fructosyl-amino acid oxidase taught in Hourichi et al. It goes without saying that an amino acid is structurally and chemically distinguishable from an amine. With respect to the classification number E.C. 1.5.3, apparently relied upon by the Patent Office, this merely represents a very broad classification in which enzyme in this class of enzymes that are acting on the CH-NH group of donors, and where oxygen is an acceptor in the catalyzed reaction. (see *Enzyme Nomenclature 1992*, Academic Press, San Diego, California, ISBN 0-12-227164-5]; http://www.chem.qmul.ac.uk/iubmb/enzyme/EC1/cont1b.html).

The substrates for the two enzymes are also different. With reference to Figure 1 of the instant application, "fructosamine" is shown to be a substrate for fructosamine oxidase. Hourichi et al. teaches that the substrates for its enzyme are "Fructosyl-glycine + $O_2$ + $H_2O$" (see page 108, equation). Not surprisingly, the names of the two enzymes are indicative of the substrates

they act upon. In the Abstract, Hourichi et al. states: "Fructosyl-α-L-amino acid" was the substrate having the highest susceptibility to the enzyme, but N-fructosyl derivatives of other materials, such as B-amino acids, L-imino acids, D-amino acids, alkyl amines, and ammonia, showed almost no susceptibility." Under the section "Substrate specificity", the authors of Hourichi et al. elaborate in stating the following: "As seen with glucitonyl, the carbonyl group in its fructosyl residue is indispensable to the enzyme reaction."(emphasis added). With reference to Figure 1 of the instant specification, the fructosamine substrate for fructosamine oxidase of claim 27 does not have a carbonyl group.

Lastly, the reaction products formed by the two enzymatic reactions are different. With reference to Figure 1 of the instant application, "α-dicarbonyl" and "reduced enzyme/protein complex" are shown to be products of the fructosamine oxidase catalyzed reaction. Hourichi et al. teaches that the reaction products for its enzyme are "Glucosone + Glycine + $H_2O_2$" (see page 108, equation).

It should thus be readily apparent to one of skill in the art that the fructosamine oxidase of claim 27 and the enzyme described in Hourichi et al. are different enzymes. The enzymes have different names (nomenclature), different substrates, and different reaction products. Accordingly, any method of determining enzymatic activity that might be taught in Hourichi et al. is for a different enzyme and thus does not anticipate the method of determining a level of fructosamine oxidase activity of claim 27, which comprises that step of measuring conversion of a substrate to a product by fructosamine oxidase.

It is well settled law that "[a]nticipation requires the disclosure in a single prior art reference of each element of a claim under consideration." *W.L. Gore & Associates v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). It is

also well settled that the burden of establishing a *prima facie* case of anticipation resides with the Patent and Trademark Office. *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984); *In re Warner*, 379 F.2d 1011, 1016, 154 USPQ 173, 177 (CCPA 1967). The Federal Circuit has elaborated that "[i]f the examination at the initial stage does not produce a prima facie case of unpatentability, then without more the Applicant is entitled to a grant of patent." *In re Oetiker*, 977 F.2d 1443, 24 USPQ 2d 1443 (Fed. Cir. 1992).

In lieu of the deficiencies of Hourichi et al., Applicant respectfully requests that the rejection of claims 27-29, 34 and 35 under 35 U.S.C. §102(b) be reconsidered and withdrawn.

## CONCLUSION

For the reasons set forth above, Applicant respectfully submits that all remaining claims in the application are now in condition for allowance. The Examiner is encouraged to contact the undersigned if it is believed this would expedite prosecution.

Please charge Deposit Account No. 02-4553 the fee of $475.00 for a three-month extension of time. No additional fees are believed to be due at this time; however, if any fee should become due or credit become payable during the pendency of these proceedings, the Commissioner is authorized to charge or credit the same to Deposit Account No. 02-4553.

Respectfully submitted,

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